

Applicants have amended Claims 172-177, 180-188 to change the term "discrete known regions" to "positionally defined locations". Applicants have amended Claims 189, 192, 202-206, 208 and 212 to change the term "known location" to "positionally defined location". Support for this amendment can be found throughout the Specification, for example, at page 4, lines 5-8.

No new matter is added by these amendments.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Theresa A. Devlin
Theresa A. Devlin
Registration No. 45,361
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133

Dated: 2/5/02

COPY OF PAPERS
ORIGINALLY FILEDMARKED UP VERSION OF AMENDMENTSSpecification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Please replace the paragraph 1 on at page 1 with the paragraph below marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

The present application is a continuation of [09/557,874,] U.S.S.N. 09/557,875 filed April 24, 2000, which is a continuation of U.S.S.N. 09/056,927 filed April 8, 1998, which is a continuation of U.S.S.N. 08/670,118 filed June 25, 1996, (now [US] U.S. 5,800,992), which is a divisional of U.S.S.N. 08/168,904 filed December 15, 1993, which is a continuation of U.S.S.N. 07/624,114, filed December 6, 1990 (all incorporated by reference), which is a continuation-in-part of commonly assigned patent applications Pirrung *et al.*, U.S.S.N. 07/362,901 (VLSIPS parent) filed on June 7, 1989; and Pirrung *et al.*, U.S.S.N. 07/492,462 (VLSIPS CIP), filed on March 7, 1990 (now [US] U.S. 5,143,854), which are hereby incorporated herein by reference. [09/557,874] The present application is also a continuation-in-part of [USSN] U.S.S.N. 08/348,471 filed November 30, 1994, which is a continuation of [USSN] U.S.S.N. 07/805,727 filed December 6, 1991 (now [US] U.S. 5,424,186), which is a [continuation in part] continuation-in-part of [USSN] U.S.S.N. 07/624,120, filed December 6, 1990, which is a continuation-in-part of [USSN] U.S.S.N. 07/492,462, filed March 7, 1990 (now [US] U.S. 5,143,854), which is a continuation-in-part of [USSN] U.S.S.N. 07/362,901, filed June 7, 1989. Additional commonly assigned applications Barrett *et al.*, U.S.S.N. 07/435,316 (caged biotin parent) filed November 13, 1989; and Barrett *et al.*, U.S.S.N. 07/612,671 (caged biotin CIP), filed November 13, 1990 are also incorporated herein by reference. Additional applications Pirrung *et al.*, U.S.S.N. 07/624,120 (now abandoned) a divisional of which has issued as [US] U.S. 5,744,101 and Dower *et al.*, U.S.S.N. 07/626,730 (now [US] U.S. 5,547,839), which are also commonly assigned and filed on the same day as this application, are also hereby incorporated herein by reference.

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

172. (Amended) A substrate with a surface comprising a plurality of polypeptides with different, known sequences bound to the surface in [discrete known regions] positionally defined locations, at a density exceeding 400 different polypeptides occupying a total area of less than 1 cm² on said substrate, said groups of polypeptides having different polypeptide sequences.
173. (Amended) The substrate as recited in claim 172, wherein said substrate comprises 10³ or more different groups of polypeptides with known sequences bound to [discrete known regions] positionally defined locations of said substrate.
174. (Amended) The substrate as recited in claim 172, wherein said substrate comprises 10⁴ or more different groups of polypeptides with known sequences bound to [discrete known regions] positionally defined locations of said substrate.
175. (Amended) The substrate as recited in claim 172, wherein said substrate comprises 10⁵ or more different groups of polypeptides with known sequences in [discrete known regions] positionally defined locations.
176. (Amended) The substrate as recited in claim 172, wherein said substrate comprises 10⁶ or more different groups of polypeptides with know sequences in [discrete known regions] positionally defined locations.
177. (Amended) The substrate as recited in claims 172, wherein said groups of polypeptides are at least 50% pure within said [discrete known regions] positionally defined locations.
180. (Amended) A substrate with a surface comprising a plurality of polypeptides with different, known sequences bound to the surface in [discrete known regions] positionally defined locations, at a density exceeding 1000 different polypeptides occupying a total area of less

than 1 cm² on said substrate, said groups of polypeptides having different polypeptide sequences.

181. (Amended) The substrate as recited in claims 180, wherein said substrate comprises 10³ or more different groups of polypeptides with known sequences bound to [discrete known regions] positionally defined locations of said substrate.
182. (Amended) The substrate as recited in claim 180, wherein said substrate comprises 10⁴ or more different groups of polypeptides with known sequences bound to [discrete known regions] positionally defined locations of said substrate.
183. (Amended) The substrate as recited in claim 180, wherein said substrate comprises 10⁵ or more different groups of polypeptides with known sequences in [discrete known regions] positionally defined locations.
184. (Amended) The substrate as recited in claim 180, wherein said substrate comprises 10⁶ or more different groups of polypeptides with known sequences in [discrete known regions] positionally defined locations.
185. (Amended) An array of more than 1,000 different groups of polypeptide molecules with known sequences bound to a surface of a substrate, said groups of polypeptide molecules each in [discrete known regions] positionally defined locations and differing from other groups of polypeptide molecules in monomer sequence, each of said [discrete known regions] positionally defined locations being an area of less than about 0.01 cm² and each [discrete known region] positionally defined locations comprising polypeptides of known sequence, said different groups occupying a total area of less than 1 cm².
186. (Amended) The array as recited in claim 185, wherein said [discrete known region] positionally defined locations is less than about 1x10⁻² cm² to about 1x10⁻⁵ cm².

187. (Amended) The method as recited in claim 186, wherein said [discrete known region] positionally defined locations is less than about $1 \times 10^{-2} \text{ cm}^2$ to about $1 \times 10^{-4} \text{ cm}^2$.
188. (Amended) The method as recited in claim 187, wherein said [discrete known region] positionally defined locations is less than about $1 \times 10^{-2} \text{ cm}^2$ to about $1 \times 10^{-3} \text{ cm}^2$.
189. (Amended) The array as recited in claim 185, made by the process of:
- a) providing a polypeptide array comprising at least two different polypeptides immobilized on a surface, and wherein said polypeptides are synthesized on said surface;
 - b) contacting said surface with a first protected amino acid wherein said first protected amino acid is selectively coupled to a functional group in a first selectively activated region of said surface;
 - c) contacting said surface with a second protected amino acid without physical segregation of said surface such that said second protected amino acid is selectively coupled to a functional group in a second selectively activated region of said surface; and,
 - d) repeating the above steps until at least two different polypeptides are formed at [known locations] positionally defined locations on said substrate surface.
192. (Amended) An array of polypeptides, said array of polypeptides comprising:
- a substrate having a surface; and
 - a plurality of different polypeptides bound to said surface at a density exceeding 400 different polypeptides/ cm^2 , wherein each of said plurality of different polypeptides is attached to said surface in a different [known] positionally defined location of area greater than 100 square microns, has a different determinable sequence.
202. (Amended) The array of claim 192, wherein each of said different [known] positionally defined locations is physically separated from each of the other [known] positionally defined locations.

203. (Amended) The array of claim 192, wherein said polypeptides in said different [known] positionally defined locations comprise polypeptides that are at least 20% pure.
204. (Amended) The array of claim 192, wherein said polypeptides in said different [known] positionally defined locations comprise polypeptides that are at least 50% pure.
205. (Amended) The array of claim 192, wherein said polypeptides in said different [known] positionally defined location are at least 80% pure.
206. (Amended) The array of claim 192, said polypeptides in said different [known] positionally defined locations are at least 90% pure.
208. (Amended) The array of claim 192, wherein said polypeptides in said different [known] positionally defined locations are at least 10% pure.
212. (Amended) The array of claim 210, wherein said plurality of different polypeptides exceeds 1000 different groups wherein each of said plurality of different polypeptides is attached to said surface in a different [known] positionally defined location of area greater than 100 square microns, has a different determinable sequence.